7. Second Supplemental Information Disclosure Statement and List of References Cited by Applicant, listing references CY-DF, with copies of references CY- DF;

8. Transmittal of Revocation and Power of Attorney with Power of Attorney executed by Kathleen A. Denis Ph.D. on behalf of the Rockefeller University; and

9. Change of Correspondence Address.

IN THE CLAIMS:

Please amend the claims as follows:

Please cancel claims 1-15 without prejudice.

Please amend claim 16 to read as follows:

16 (once amended). A method for treating dopamine dysregulation in an individual in need of such treatment comprising administering to the individual an agent that inhibits the phosphorylation of Thr75-DARPP-32.

Please add new claim 22 as follows:

22 (new). The method of Claim 19, wherein the agent binds to Cdk5.

REMARKS

1. THE AMENDMENTS TO THE CLAIMS

Before this Amendment, claims 1-21 were pending. Claims 16-22 will be pending and under active consideration upon entry of this Amendment. Claims 1-15 have been canceled without prejudice as drawn to non-elected subject matter. Applicants expressly reserve the right to prosecute claims drawn to any subject matter canceled or removed by amendment in related applications.

Claim 16 has been amended to remove non-elected subject matter and new claim 22 has been added to more particularly point out and distinctly claim the subject matter of certain embodiments of the invention. No new matter is added by these amendments, and they are believed to place the claims in condition for allowance. The subject matter of the claims, as

amended, is fully supported in the specification and claims as originally filed. Accordingly, entry thereof into the instant application is respectfully requested.

In particular, claim 16 has been amended to remove non-elected subject matter, *i.e.*, to delete the recitation of an agent that promotes the dephosphorylation of Thr75-DARPP-32. Claim 16 has also been amended to recite "an individual in need of such treatment" and to substitute the word "individual" for the word "patient." Support for this amendment to claim 16 may be found, *inter alia*, at page 10, lines 11-14 and at page 24, lines 4-12.

New claim 22 has been added. Support for new claim 22 may be found at page 26, lines 15-28.

A marked up version of the claims showing the amendments made herein is attached hereto as Appendix A. A clean copy of the claims that will be pending upon entry of the amendments made herein is attached as Appendix B

2. THE RESTRICTION REQUIREMENT

Applicants hereby affirm the election with traverse of Group V, claims 16-21. Applicants also acknowledge the Examiner's note at page 2 of the Office Action that claims 16-18 will be examined to the extent they read on the elected invention. Claims 1-15 have been withdrawn from further consideration by the Examiner as drawn to non-elected inventions. Applicants have canceled the withdrawn claims and reserve the right to prosecute the subject matters of the non-elected claims in one or more related applications.

3. CLAIM OBJECTIONS

Claims 16-18 are objected to as reciting a non-elected invention. Claim 16 has been amended to delete the word "either" and the phrase "or promotes the dephosphorylation of Thr75-DARPP-32," thus obviating the objection.

4. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF ENABLEMENT SHOULD BE WITHDRAWN

Claim 16 (and claims 17-21 depending therefrom) are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. The Examiner alleges that the specification is not enabling for the claimed invention because there is no evidence of record to indicate that an agent that inhibits DARPP-32 at Threonine-75 ("Thr75-DARPP-32") would treat any

disease and neither the specification nor the art of record teaches how a skilled artisan would practice the claimed methods without undue experimentation (Office Action, page 3).

In response, Applicants respectfully disagree. The Examiner rests his rejection on an alleged lack of correlation between an agent that inhibits phosphorylation of Thr75-DARPP-32 and the use of that agent to treat a dopamine dysregulation disease. With respect to the allegations in the Office Action, Applicants assert that the claims are enabled and that the specification fully teaches the skilled artisan how to practice the claimed methods without undue experimentation.

Applicants' reasoning in support of enablement is set forth below. Briefly, the *in vitro* methods taught in the specification for identification of compounds for use in the methods of the invention, *e.g.*, Cdk5 modulators, do work, as taught, to identify such compounds, and furthermore, the use of the art-accepted animal model of a dopamine dysregulation disease taught in the specification demonstrates and verifies that compounds identified via such *in vitro* methods indeed work to treat a dopamine dysregulation disease. As discussed hereinbelow and in the Declaration of Allen A. Fienberg, Ph.D. Under 37 C.F.R. § 1.132 ("the Fienberg Declaration") filed concurrently herewith, there is indeed a correlation between the *in vitro* biochemical results described in the specification and *in vivo* results, using the animal model, showing treatment of a dopamine dysregulation disease. This correlation is demonstrated in the specification (at Example 2, pages 61-67), in which a compound identified via the *in vitro* methods, roscovitine, is demonstrated to treat a dopamine dysregulation disease in an art-accepted rat model for such a disease. Hence the teachings of the specification would have enabled the skilled artisan to practice the methods of the invention without undue experimentation.

a. The Legal Standard

The test for enablement is whether one skilled in the art could make and use the claimed invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988). Indeed, subject matter that is well known to the skilled artisan is preferably omitted from the specification. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well known in the art"). A

considerable amount of experimentation is permitted if it is merely routine or if the specification provides reasonable amount of guidance and direction to the experimentation. *In re Jackson*, 217 U.S.P.Q. 804, 807 (1982). Further, one skilled in the art is presumed to use the information available to him in attempting to make and use the claimed invention. *See Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990) ("A decision on the issue of enablement requires determination of whether a person skilled in the pertinent art, using the knowledge available to such a person and the disclosure in the patent document, could make and use the invention without undue experimentation."). These enablement rules preclude the need for the patent applicant to "set forth every minute detail regarding the invention." *Phillips Petroleum Co. v. United States Steel Corp.*, 673 F. Supp. 1278, 1291 (D. Del. 1991); *see also DeGeorge v. Bernier*, 768 F.2d 1318, 1323 (Fed. Cir. 1985).

A disclosure adequately fulfills the enablement requirement if it defines the desired functional relationship. *Wilden Pump & Eng'r Co. v. Pressed & Welded Prod. Co.*, 199 U.S.P.Q. 390 (N.D. Cal. 1978), *aff'd,* 655 F.2d 984, 213 U.S.P.Q. 282 (9th Cir. 1981), *on remand*, 570 F.Supp. 224, 224 U.S.P.Q. 1074 (N.D. Cal. 1983) ("A patent's disclosure is adequate if it defines the desired functional relationship, even if some experimentation is required to reproduce the invention."). *See also, S.C. Johnson & Son, Inc. v. Carter-Wallace, Inc.*, 225 U.S.P.Q. 1022 (S.D.N.Y. 1985); *aff'd in part, vacated in part, and remanded,* 781 F.2d 198, 228 U.S.P.Q. 367 (Fed. Cir. 1986), *on remand,* 231 U.S.P.Q. 668 (S.D.N.Y. 1986) ("There is no need for a manufacturing specification. There need not be a description of every nut, bolt and detail used in the practice of the invention."); *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (U.S. Int'l Trade Comm. 1983), *aff'd sub nom., Massachusetts Institute of Technology v. AB Fortia*, 774 F.2d 1104, 227 U.S.P.Q. 428 (Fed. Cir. 1985) ("[T]he fact that experimentation may be complex . . . does not necessarily make it undue, if the art typically engages in such experimentation.").

While the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of an experiment is not a consideration. Indeed, the Court of Customs and Patent Appeals has specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue. *In re Angstadt,* 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). With respect to unpredictable methods, the *Angstadt* court further stated:

> Appellants have apparently not disclosed *every* catalyst which will work; they have apparently not disclosed *every* catalyst which will not work. The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with *every* species covered by a claim.
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> * * *
>
> [S]uch a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area . . . .

Id. (emphasis in original). The *Angstadt* court held that applicants had indeed enabled their method for catalytically oxidizing hydrocarbons, explaining:

> [T]he proposition that the disclosure must provide "guidance which will enable one skilled in the art to determine, *with reasonable certainty before performing the reaction*, whether the claimed product will be obtained" . . . is contrary to the basic policy of the Patent Act, which is to encourage disclosure of inventions and thereby to promote progress in the useful arts.
>
> * * *
>
> Depriving inventors of claims which adequately protect them and limiting them to claims which practically invite appropriation of the invention while avoiding infringement inevitably has the effect of suppressing disclosure.

Id., *quoting and criticizing In re Rainer*, 54 C.C.P.A. 1445, 377 F.2d 1006, 153 U.S.P.Q. 802 (1967) (emphasis in original).

b. The Specification Provides Sufficient Guidance for Identification of Agents for Use in the Methods of the Invention and for Using the Agents in the Methods of the Invention

The Examiner asserts that it is questionable whether a compound that inhibits the phosphorylation of Thr75 of DARPP-32 could be used to treat a dopamine dysregulation related disease and alleges that "at the time of the invention[,] dopamine mediated signal transduction was not clear in the art and therefore, an artisan of skill would have [been] required [to conduct] extensive experimentation to treat any condition of dopamine dysregulation with any agent" (Office Action, page 4). Applicants emphatically disagree.

In certain embodiments, the invention provides a method for treating dopamine dysregulation in a patient comprising administering to the patient an agent that either inhibits

the phosphorylation of Thr75-DARPP-32 or promotes the dephosphorylation of Thr75-DARPP-32. In particular, certain embodiments of the invention are drawn to a method for treating dopamine dysregulation in a patient comprising administering to the patient an agent that inhibits the phosphorylation of Thr75-DARPP-32 by Cdk5.

At page 4 of the Office Action, the Examiner alleges a lack of correlation between experimental outcomes of *in vitro* and *in vivo* assays. Applicants respectfully disagree. As discussed in the Fienberg Declaration at paragraphs 6-20, as of the claimed priority date of the application, the skilled artisan, armed with the teachings of the specification and with what was routinely known in the art at that time, could have (a) identified compounds that modulate, *e.g.*, inhibit, the phosphorylation of Thr75-DARPP-32, *e.g.*, by Cdk5, and (b) these compounds could have been routinely tested *in vivo* in an art-accepted animal model and shown to treat a dopamine dysregulation disease, as was demonstrated in the specification at Example 2. For example, at paragraph 8, Dr. Fienberg states that:

> the specification teaches . . . that alternatively, or in conjunction with *in vitro* assays, an animal model can be used to ascertain the effect of a potential agent on a dopamine-related condition and that a potential modulator that ameliorates the dopamine-related condition can then be selected. It would have been recognized by the skilled artisan, from the teachings in the specification, that an animal model can thus be used to corroborate the results of the *in vitro* brain slice assay as taught in the specification, and to corroborate the effect of a potential agent on a dopamine dysregulation disease.

Fienberg Declaration, paragraph 8 (emphasis added).

The Examiner rests his rejection on an alleged lack of correlation between an agent that inhibits phosphorylation of Thr75-DARPP-32 *in vitro* and the use of that agent to treat a dopamine dysregulation disease *in vivo*. Applicants draw the Examiner's attention to the specification, which teaches at page 29, lines 3-11, and at pages 58-59, that an art-accepted *in vitro* assay, the mouse striatal brain slice assay, may be used to assay for the phosphorylation of Thr75-DARPP-32 by Cdk5. Furthermore, as taught in the specification, roscovitine, a compound identified via *in vitro* methods to inhibit phosphorylation of Thr75-DARPP-32 (see Example 1, at pages 57-60) was demonstrated to treat a dopamine dysregulation disease in an art-accepted animal model for such a disease (see Example 2, at pages 61-67 and Fienberg Declaration at paragraphs 9-10).

c. The Animal Model Taught in the Specification Was an Art-Accepted Model for a Dopamine Dysregulation Disease

The Examiner alleges that "even if there is an effect of an agent in vitro, [the] same effect may not be observed in vivo" (Office Action, page 4). The MPEP states that "if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate." M.P.E.P. § 2164.02. In the present case, the Examiner has not provided any evidence that the model does not correlate.

Applicants assert that, as discussed in the Fienberg Declaration at paragraphs 8-16, it was well within the skill of a skilled artisan to routinely verify that an agent that had an effect *in vitro* also had an effect *in vivo* using an art-accepted animal model, a rat model for a dopamine dysregulation condition (produced by chronic administration of cocaine). As discussed above and in paragraph 8 of the Fienberg Declaration, Dr. Fienberg states that a skilled artisan would recognize, from the teachings in the specification, "that an animal model can thus be used to corroborate the results of the *in vitro* brain slice assay as taught in the specification, and to corroborate the effect of a potential agent on a dopamine dysregulation disease."

Applicants also assert that, as discussed in the Fienberg Declaration at paragraphs 8-19, experimental results using this rat model were routinely correlated to experimental outcomes in human patients. In particular, at paragraph 17 of the Fienberg Declaration, Dr. Fienberg states that, based on experimental results obtained from animal models, "it was also well within the skill of a skilled artisan to select dosage regimens for testing in clinical trials . . . and subsequently, to select a dosage regimen based on the results of the clinical trial."

Applicants further assert that, as discussed in the Fienberg Declaration at paragraph 16, it was well within the skill of a skilled artisan, as of the claimed priority date of the invention, to select a potential agent whose effects in humans were previously unknown and to determine whether it could be used to inhibit Thr75-DARPP-32 phosphorylation and to treat a dopamine dysregulation disease. Using the methods taught in the specification, moreover, a skilled artisan would have been enabled to routinely identify other compounds useful for practicing the methods of the invention, *e.g.*, other members of the indirubin or paullone families, which would have been expected to be useful in treating a dopamine

dysregulation disease as taught in the specification (see Office Action at page 5 and Fienberg Declaration at paragraph 16).

d. The Methods of the Invention May be Used to Treat a Dopamine Dysregulation Condition Modulated by D1 or D2 Receptor Activation

At page 4 of the Office Action, the Examiner cites Bibb *et al.* (1999, Nature 402:669-671, Ref. CX of record)[1] as disclosing that "Cdk5 phosphorylates Thr75-DARPP-32 using a DARP[P]-32 mutant mouse brain slice or purified protein," but that "[s]ince dopamine acts via D1 receptors which in turn act via PKA and DARPP-32, even if an agent had [an] effect in vitro on DARPP-32, it would not affect D2 type receptors and therefore, a DARPP-32 phosphorylation inhibitor would not treat a condition that is due to dysregulation of dopamine function via D2 receptors" (emphasis added). Applicants respectfully disagree.

Dopamine is recognized by the skilled artisan to achieve many, but not all, of its effects in neurons by activating the D1 class of dopamine receptors, which are positively coupled to the activation of PKA (see for review, Greengard *et al.*, 1999 (July), Beyond the dopamine receptor: the DARPP-32/protein phosphatase-1 cascade, Neuron 23: 435-47, Ref. DA of record, submitted concurrently herewith in a Second Supplemental Information Disclosure Statement). At the time the application was filed, however, it was well known in the art that phosphorylation of DARPP-32 was bidirectionally regulated by dopamine and by both dopamine D1 and D2 receptors (PCT publication WO 99/20273 by Nishi *et al.*, published April 29, 1999, Ref. CZ of record, "Nishi I"; and U.S. Patent No. 6,013,621, by Nishi *et al.*, issued January 11, 2000, Ref. CY of record, "Nishi II,"both submitted concurrently herewith in a Second Supplemental Information Disclosure Statement). The skilled artisan would have recognized that dopamine binds to and modulates that activity of both D1 and D2 receptors and that both D1 and D2 intracellular signaling pathways are modulated via the modulation of the intracellular signaling molecule DARPP-32 (*see, e.g.*, page 436 and Figure 1 of Greengard *et al.*, 1999, Ref. DA of record; *see also* Greengard *et al.*, 2001, Science 294:1024-1030, Ref. U of record [2]). Hence, the skilled artisan would have

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[1]Note that there is an apparent typographical error in the Office Action, which cites this reference as "Fienberg *et al.* (1999, Nature 402:669-671)."

[2] Note that there is an apparent typographical error in the Office Action, which cites this (continued...)

recognized that dysregulation of either D1 or D2 intracellular signaling pathways would be potentially ameliorated by modulating the phosphorylation of DARPP-32.

For example, it was well-known in the art, as of the claimed priority date, that dysregulation of the activity of either an element upstream or downstream of a particular element in an intracellular signaling pathway would lead to dysregulation of activity of the pathway as a whole. Hence, it would be instantly recognized by one of skill in the art that dysregulation of the activity of either an element upstream or downstream of DARPP-32, and in either the dopamine D1 or D2 receptor intracellular signaling pathway, will lead to dysregulation of activity of the pathway as a whole (see, *e.g.*, Figure 1 of Greengard *et al.*, 1999, Ref. DA of record, for a diagram showing these art-recognized intracellular signaling pathways). Hence, an agent that has an effect *in vitro* (or *in vivo*) on the phosphorylation of DARPP-32 would have been recognized by the skilled artisan as necessarily affecting the regulation of both D1 and D2 intracellular signaling pathways.

Furthermore, as stated in the Fienberg Declaration at paragraph 18, the specification teaches the use of an agent that modulates a dopaminergic intracellular signaling pathway by inhibiting the phosphorylation of Thr75-DARPP-32 or promoting the dephosphorylation of Thr75-DARPP-32 (page 10, lines 11-15). As of the claimed priority date, skilled artisans recognized that the modulation of DARPP-32 phosphorylation would necessarily modulate the activity of a dopaminergic intracellular signaling pathway, whether or not it also modulated other signal transduction pathways, *e.g.*, NMDA, AMP, GAB VIP, 5HT4 or A2A intracellular signaling pathways. Armed with such knowledge, a skilled artisan could have practiced the claimed methods of the invention and, indeed, determined whether "the effect [of a potential agent would] be there in vivo" (Office Action at page 5) and whether administration of the agent would produce an ameliorative effect in a patient.

At page 5, the Office Action cites Greengard *et al.*, 2001 (Ref. U of record) as disclosing that DARPP-32 phosphorylation is a complex cascade of events, and states that "it is not clear as to how the effect of an agent on [DARPP]-32 would be targeted only to one site since [the] same mechanism of signal transduction may be used by multiple molecules and therefore, an agent that inhibits DARPP-32 would not specifically affect dopamine mediated functions." Applicants submit that the disclosure adequately fulfills the enablement

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[2](...continued)
reference as "Greengard (Science 281:838-1030)."

requirement by disclosing how to assay for modulation of dopamine mediated functions, and how to correlate biochemical results obtained *in vitro* with results, *e.g.*, behavioral results, obtained in an animal model *in vivo*, even if some experimentation is required to reproduce the invention.

The Examiner cites Fienberg *et al.* (1998, Science 281:838-842, Ref. AK of record), Snyder *et al.* (J. Neurosci. 12:3071-3083, Ref. CH of record), Hemmings *et al.* (1989, J. Biol. Chem. 264: 7726-33, Ref. AU of record), Girault *et al.* (1989, J. Biol. Chem. 264: 21748-59, Ref. AO of record) as teaching *in vitro* methods of using brain slices for phosphorylation assays of DARPP-32 and other substrates, but alleges that "prior arts on record do not teach the method for treating any diseases or conditions with agents that inhibit DARPP-32 or Cdk5" (Office Action at page 5). Applicants respectfully disagree. The Fienberg Declaration (at paragraph 15) discusses U.S. Patent No. 5,777,195 (issued July 7, 1998 to Fienberg *et al.*, Ref. CW of record) and other references that disclose that, as of the claimed priority date, results from mouse brain slice assays were routinely correlated with results from *in vivo* assays, to predict the potential ameliorative effects of an agent on dopaminergic dysregulation in a human patient.

e. It Would Have Been Routine for a Skilled Artisan to Practice the Methods of Treatment of the Invention for Inhibiting DARPP-32 or Cdk5

The Examiner also alleges that it would have been undue experimentation for an artisan to practice the claimed method of treatment because neither the prior art nor the specification teaches how to treat a patient by administering an inhibitor of DARPP-32 or Cdk5 (Office Action at page 7). Applicants respectfully disagree. Applicants assert that, contrary to the Examiner's allegation, armed with the teaching of the specification, the skilled artisan would be readily able to adapt methods commonly known in the art to practice the methods of the invention for treating dopamine dysregulation in a patient. As discussed in the Fienberg Declaration at paragraph 15, such correlation, as taught in the specification, of an *in vitro* brain slice assay with an *in vivo* assay in an animal model, *e.g.*, a locomotor assay in a rodent model, was accepted by skilled artisans, as of the claimed priority date, as an experimental approach that is directly predictive of the potential ameliorative effects of an agent of interest on dopaminergic dysregulation in a human patient.

Finally, at page 7 of the Office Action, the Examiner alleges that it is not clear what would be the outcome of treating a dopamine dysregulation condition by giving a patient a Cdk5 inhibitor. As discussed in the Fienberg Declaration at paragraphs 8-19, the specification teaches that *in vitro* assays (*e.g.*, mouse striatal brain slice taught in the specification at Example 1) and *in vivo* assays (*e.g.*, the rat model taught in the specification at Example 2) may be used to predict an experimental or clinical outcome in a human patient. Applicants submit that, as discussed above, unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue. *In re Angstadt,* 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976).

According to the applicable case law discussed above, under 35 U.S.C.§ 112, an invention is enabled even though the disclosure may require some routine experimentation to practice the invention. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). Considerable amount of experimentation is permitted if it is merely routine or the specification provides reasonable amount of guidance and direction to the experimentation. *In re Jackson*, 217 U.S.P.Q. 804, 807 (1982).

The specification fully teaches how to carry out, under routine conditions, *in vitro* assays to evaluate potential agents to treat a dopamine dysregulation disease and how to confirm, using *in vivo* assays in a rat model for dopamine dysregulation, that the potential agent indeed treats the disease. Where a disclosure provides considerable direction and guidance on how to practice the invention, and where, at the time of the application, the skill in the art was quite high and the methods needed to practice the invention well known, a conclusion of enablement should be made. *In re Wands*, 858 F.2d 731, 740, 8 U.S.P.Q.2d. 1400, 1406 (Fed. Cir. 1988). Here, the specification provides reasonable amount of guidance and direction for practicing the claimed method without undue experimentation, hence the invention is enabled.

CONCLUSION

It is submitted, based on the foregoing, that the above rejections of claims 16-21 under 35 U.S.C. § 112, first paragraph, for lack of enablement, have been obviated. Accordingly, Applicants respectfully request that these rejections be reconsidered and withdrawn. Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the present application. Withdrawal of the Examiner's

rejections and a notice of allowance are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: September 30, 2002

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Enclosures

APPENDIX A

Marked Up Version of the Amended Claims

U.S. Patent Application Serial No. 09/687,959

Matter that has been deleted from the claims is indicated by brackets and matter that has been added to the claims is indicated by underlining.

16 (once amended). A method for treating dopamine dysregulation in an individual in need of such treatment comprising administering to the [patient] individual an agent that [either] inhibits the phosphorylation of Thr75-DARPP-32[or promotes the dephosphorylation of Thr75-DARPP-32].

APPENDIX B

Claims Pending upon Entry of the Present Amendments

U.S. Patent Application Serial No. 09/687,959

16 (once amended). A method for treating dopamine dysregulation in an individual in need of such treatment comprising administering to the individual an agent that inhibits the phosphorylation of Thr75-DARPP-32.

17. The method of Claim 16, wherein the dopamine dysregulation leads to a symptom characteristic of a condition selected from the group consisting of schizophrenia, Parkinson's Disease, Tourette's syndrome, Huntington's disease, attention deficit hyperactivity and drug abuse.

18. The method of Claim 16, wherein the agent can cross the blood brain barrier.

19. The method of Claim 16 wherein the phosphorylation of Thr75-DARPP-32 is inhibited by inhibiting Cdk5.

20. The method of Claim 19 wherein the agent is roscovitine.

21. The method of Claim 19 wherein the agent is a member of the class of compound selected from the group consisting of an indirubin and a paullone.

22 (new). The method of Claim 19, wherein the agent binds to Cdk5.